

**REMARKS**

Claims 1-45 were pending in this application. Claims 16, 17, 25, 26, 31-40, 43 and 44 have been withdrawn from consideration. Claims 31-34 have been canceled without prejudice. Applicants may pursue this subject matter in one or more divisional applications. Claim 1 has been amended to specify that the component associated with the gas-filled microvesicle is substantially free of magnetic particles. This amendment is supported throughout the specification, particularly at Examples 10a-b, 12a-b, 14a-b, 15, 16, 17, 18, 19, 20, 22, 23, 24, 25, 26 and paragraphs 0134, 0203 0052 . New claims 46-49 have been added, directed to an assembly in which the component associated with the microvesicle is a supermolecular structure formed by the association of a plurality of molecules, which bears a second overall net charge opposite in sign to said first net charge, consists essentially of molecules of a biocompatible surface active agent, optionally comprises a targeting ligand and/or a bioactive agent and has a diameter of 100 nm or lower. Support for this subject matter is found throughout the specification, particularly at paragraph 0134, paragraphs 0169- 0181, paragraphs 0047 and 0048, 0061, 0062, 0052 and in the original claims. No new matter has been added. Thus, claims 1-30, 35-49 are now pending and claims 16, 17, 25, 26, 35-40, 43 and 44 have been withdrawn. Applicants reiterate their request for rejoinder of dependent method claims 35-40, 43 and 44 at the appropriate time.

**Double Patenting**

Applicants are grateful for the withdrawal of the double patenting rejection over USSN 10/584,382.

**Rejections Under 35 U.S.C. § 103**

Applicants are grateful for the withdrawal of the rejection of claims 1, 4-15, 18, 19, 27-30 and 42 for alleged obviousness over Eriksen US 2004/0146462. Applicants are also grateful for the withdrawal of the rejection of claims 1-15, 18-24, 27-30, 41, 42 and 45 for alleged obviousness over Schneider et al US 6,528,378 in view of Eriksen US 2004/0146462 and further in view of Unger US 2002/0159952.

**Rejection for Alleged Obviousness Over JP 2000143550 in view of WO 03/05029 and,  
Optionally, other Secondary References**

Claims 1-12, 18, 19, 27-30, 41, 42 and 45 were rejected for alleged obviousness JP 2000143550 in view of WO 03/05029. Claims 1-12, 18-24, 27-30, 41, 42 and 45 were rejected for alleged obviousness over JP 2000143550 in view of WO 03/05029 and further in view of Bao US2005/0130167. Claims 1-15, 18, 19, 27-30, 41, 42 and 45 were rejected for alleged obviousness over JP 2000143550 in view of WO 03/05029 and further in view of Dugstad US 6,221,337 (“Dugstad”).

The Examiner found that JP 2000143550 teaches magnetic particles adsorbed on the surface of microvesicles coated with a carboxylic acid salt which are preferably coated with a cationic surfactant. JP 2000143550 teaches that the movement of the contrast agent can be controlled by an external magnetic field. Although the Examiner concedes that the magnetic particles associated with the microbubbles in the examples of JP 2000143550 are 300 nm rather than 100nm or less as claimed, she asserts that “[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to modify particle size of the magnetic particles taught by JP 2000143550 which are used for magnetically guiding the microbubbles, to employ a particle size such as 50 nm. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so because WO 03/05029 shows that particles in the range of 50-150 nm are preferable for use in magnetic drug delivery or biological cell separation.” OA at p. 4-5.

Applicants respectfully traverse. The currently pending claims, and in particular independent claims 1 and 46 require that the component associated with the microvesicle is substantially free of magnetic particles or consists essentially of molecules of a biocompatible surface agent (and optionally a targeting ligand and/or bioactive agent). In contrast, as the Examiner admits, JP 2000143550 is directed exclusively to associating magnetic particles with microbubbles coated with a carboxylic salt. Thus, it neither teaches nor suggests the claimed invention. Similarly, WO 03/05029 and Bao US 2005/0130167 are directed to magnetic particles or magnetic particle probes (see e.g. WO 03/05029, p. 1, lines 10-15, p. 4, lines 5-6; Bao US 2005/0130167, abstract ). Thus, these cited references when considered in

combination neither teach nor suggest the claimed invention or its claimed advantages (discussed at paragraphs 0050-0053). Dugstad fails to remedy these deficiencies. It was cited for its disclosure of microbubbles surrounded by a layer of negatively charged phospholipid and neither teaches nor suggests the claimed assemblies when combined with the other cited references.

In sum, even when considered in combination, the cited references fail to disclose each element of the claimed invention and particularly fail to teach or suggest the claimed associated components which do not include magnetic particles.

In view of the preceding remarks, it is believed that claims 1-15, 18-24, 27-30, 41-42 and 45--48 are in condition for allowance. Applicants reiterate their request to rejoin claims 35-40, 43 and 44.

If there are any questions remaining as to patentability of the pending claims, Applicants would very much desire to have a telephonic interview. The Examiner is invited to contact Applicants' undersigned attorney at the number below.

No fee is believed to be necessary in connection with the filing of this Response other than the fee for the extension of time. However, if any additional fee is necessary, applicant hereby authorizes such fee to be charged to Deposit Account No. 50-2168.

Favorable action is respectfully requested.

Respectfully submitted,

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/M. Caragh Noone, Reg. No. 37,197/ .

M. Caragh Noone, Reg. No. 37,197  
Bracco Research USA Inc.  
305 College Road East  
Princeton, NJ 08540  
Tel: (609) 514-2454  
Fax: (609) 514-244